REMARKS

Claims 1-36 are pending in the present application. Claims 5-8 are rejected. Claims 1-4 and 9-36 are withdrawn from consideration as being drawn to a non-elected invention. Applicants herein make minor changes to claims 5 and 7 so that they read "consisting of" instead of "comprising." No issue of new matter arises by way of this change as it merely employs the art and tradition recognized patent words to more clearly define what is claimed. Further, Applicants clarify that the acetyl lysine residue is present as a residue within a peptide or protein. No issue of new matter arises by way of this change since the first sentence of the the Summary of the Invention describes very clearly this very fact.

Rejection under 35 U.S.C. § 112

Claims 5-8 are rejected under 35 U.S.C. §112, first paragraph for not fulfilling the enablement and written description requirements of the patent statute.

Regarding Enablement

The Examiner maintains the rejection of claims 5-8 as allegedly not being enabled. The Examiner notes that these claims read on peptides comprising the ZA loop of protein bromodomains that fall within an indicated generic structure, that of SEQ ID NO: 3. The claims also recite the functional limitations that the peptides are useful for screening for inhibitors of interaction between a bromodomain and an acetylated lysine.

A. Regarding the Scope of Bromodomains

The Examiner alleges that while the application may enable using the P/CAF bromodomain, the application provides little if any guidance as to the use of other bromodomains. There is no specific identification of what diseases such other bromodomains may be associated with, or what acetyl-lysine containing peptides they may interact with. Applicants previously submitted that because teachings regarding the

potential use of the P/CAF bromodomain are explicitly set forth, those skilled in the art would be able to use any ZA loop of any bromodomain. The Examiner alleges that this is not supported by the teachings of the art.

Applicants respectfully submit that the patent law does not require any number of species to describe a genus. Nonetheless, Applicants submit herewith the Declaration of Dr. Ming-Ming Zhou pursuant to 37 C.F.R. 1.132 wherein the Declarant clarifies that he is aware of many proteins containing a bromodomain that have been shown to interact with other proteins. Representative examples include the bromodomain of WSTF (Williams syndrome transcription factor) interacts with lysine-acetylated histones (Fujiki, R., et al., *Ligand-induced transrepression by VDR through association of WSTF with acetylated histones.* Embo J, 2005); the bromodomain of the transcriptional cofactor p300 binds to nucleosome (Ragvin, A., et al., *Nucleosome binding by the bromodomain and PHD finger of the transcriptional cofactor p300.* J Mol Biol, 2004. **337**(4): p. 773-88); the bromodomain of CBP/p300 binds to acetylated MyoD (Polesskaya, A., et al., *Interaction between acetylated MyoD and the bromodomain of CBP and/or p300.* Mol Cell Biol, 2001. **21**(16): p. 5312-20); the bromodomain of NoRC (the SNF2h-containing chromatin-remodeling complex) interacts with K16-acetylated histone H4 (Zhou, Y. and I. Grummt, *The PHD finger/bromodomain of NoRC interacts with acetylated histone H4K16 and is sufficient for rDNA silencing.* Curr Biol, 2005. **15**(15): p. 1434-8); the bromodomains of BDF1 and BDF2 bind to histone H4 (Matangkasombut, O., et al., *Bromodomain factor 1 corresponds to a missing piece of yeast TFIID.* Genes Dev, 2000. **14**(8): p. 951-62); the bromodomain of the WBSCR9 gene, encoding a novel transcriptional regulator, in the Williams-Beuren syndrome deletion at 7q11.23 (Peoples, R.J., et al., *Identification of the WBSCR9 gene, encoding a novel transcriptional regulator, in the Williams-Beuren syndrome deletion at 7q11.23.* Cytogenet Cell Genet, 1998. **82**(3-4): p. 238-46); the bromodomain-containing TIF1α: a possible link between KRAB zinc finger proteins and nuclear receptors (Le Douarin, B., et al., *TIF1alpha: a possible link between KRAB zinc finger proteins and nuclear receptors.* J Steroid Biochem Mol Biol, 1998. **65**(1-6): p. 43-50); the bromodomain of CBP interacts with human tumor suppressor p53 at acetylated lysine 372 (Mujtaba, S., et al., *Structural*

mechanism of the bromodomain of the coactivator CBP in p53 transcriptional activation. Mol Cell, 2004. **13**(2): p. 251-63). (*See*, Paragraph 5) In view of this wealth of information in the art, it is clear that one of skill in the art has a wealth of bromodomains at his or her disposal. As such, a skilled artisan may practice the invention without undue experimentation.

B. Regarding RING3

Furthermore, the Examiner alleges that there are no teachings in the application regarding the elected embodiments, wherein the peptide comprises the ZA loop of SEQ ID NO: 19. The Examiner admits that the art indicates that the RING3 protein, from which this sequence is derived, has some part in certain cancers. However, the Examiner contends that the relationship of the bromodomains of the protein to the cancers is not known or understood (*citing*, Denis, *et al.*, *Cell Growth Diff* 11: 417-24, at pages 417 and 422). The Examiner further admits that the art indicates that bromodomains interact with acetyl-lysine containing proteins (*citing,* Dhalluin, *et al., Nature* 399, 491-96). However, it is allegedly not clear that an inhibitor of interaction between SEQ ID NO: 19 and its (unknown, but presumably acetyl-lysine containing) ligand would inhibit or induce cancer cell growth (*citing*, Guo, *et al.*, *J Cell Sci* 113:3085-91 (it is not clear if the cancer inducing activities of RING3 are caused by up or down regulation of its ligands, and therefore it is unclear what effect inhibiting their association with RING3 would be)). The art therefore supports an assertion that the RING3 protein is associated with cancers, but indicates that the functional relationship between the cancer and the protein is unknown, and indicates uncertainty in whether an inhibitor of protein activity would inhibit or aggravate the cancer. According to the Examiner, there is no evidence in the application or indication in the art that this sequence binds to Tat, or to any HIV protein, or that inhibition between the binding of this sequence with any acetyl-lysine analog would have any effect on the progression of HIV infection.

Applicants reiterate that there is no requirement in the patent law that Applicant understand how or why an invention works. The Examiner is citing to a lack of full understanding as to mechanism of action in support of a lack of enablement. Such is not

a violation of the principles of the patent law. Nonetheless, in order to clarify the invention, Applicants herein remove the unnecessary recitations of the claims that relate the bromodomains to HIV infection or inhibition of tumor cell growth.

Applicants submit herewith the Declaration of Dr. Ming-Ming Zhou pursuant to 37 C.F.R. 1.132 wherein the Declarant clarifies that he is aware of many proteins containing a bromodomain that have been shown to interact with other proteins and for which the consequence of this interaction is understood as regards biological activity. Examples of these include that the bromodomain containing 2 (Brd2) is expressed in distinct patterns during ovarian folliculogenesis independent of FSH or GDF9 action (Trousdale, R.K. and D.J. Wolgemuth, *Bromodomain containing 2 (Brd2) is expressed in distinct patterns during ovarian folliculogenesis independent of FSH or GDF9 action.* Mol Reprod Dev, 2004. **68**(3): p. 261-8); the bromodomain of the MLL-CBP fusion protein is required for generating a myelodysplastic-like syndrome that evolves into myeloid leukemia (Lavau, C., et al., *Chromatin-related properties of CBP fused to MLL generate a myelodysplastic-like syndrome that evolves into myeloid leukemia.* EMBO J., 2000. **19**: p. 4655-4664); the bromodomain-containing histone H3 acetylase dGcn5 is a key player in Drosophila melanogaster metamorphosis(Carre, C., et al., *The histone H3 acetylase dGcn5 is a key player in Drosophila melanogaster metamorphosis.* Mol Cell Biol, 2005. **25**(18): p. 8228-38); the bromodomain protein Brd4 is a positive regulatory component of P-TEFb and stimulates RNA polymerase II-dependent transcription (Jang, M.K., et al., *The bromodomain protein Brd4 is a positive regulatory component of P-TEFb and stimulates RNA polymerase II-dependent transcription.* Mol Cell, 2005. **19**(4): p. 523-34); the PHD finger/bromodomain of NoRC interacts with acetylated histone H4K16 and is sufficient for rDNA silencing (Jang, M.K., et al., *The bromodomain protein Brd4 is a positive regulatory component of P-TEFb and stimulates RNA polymerase II-dependent transcription.* Mol Cell, 2005. **19**(4): p. 523-34); the bromodomain-containing protein Bdf1p acts as a phenotypic and transcriptional multicopy suppressor of YAF9 deletion in yeast (Bianchi, M.M., et al., *The bromodomain-containing protein Bdf1p acts as a phenotypic and transcriptional multicopy suppressor of YAF9 deletion in yeast.* Mol Microbiol, 2004. **53**(3): p. 953-68);

Bdf1 bromodomains' interactions with acetylated H4 tails help anchor the transcriptional protein complex TFIID to the promoter during the initial stages of transcription activation (Martinez-Campa, C., et al., *Precise nucleosome positioning and the TATA box dictate requirements for the histone H4 tail and the bromodomain factor Bdf1.* Mol Cell, 2004. **15**(1): p. 69-81); the CBP bromodomain and nucleosome targets are required for Zta-directed nucleosome acetylation and transcription activation (Deng, Z., et al., *The CBP bromodomain and nucleosome targeting are required for Zta-directed nucleosome acetylation and transcription activation.* Mol Cell Biol, 2003. **23**(8): p. 2633-44); the bromodomains anchor chromatin-modifying complexes to promoter nucleosomes (Hassan, A.H., et al., *Function and selectivity of bromodomains in anchoring chromatin-modifying complexes to promoter nucleosomes.* Cell, 2002. **111**: p. 369-379); the bromodomain mediates transcriptional intermediary factor 1alpha -nucleosome interactions (Remboutsika, E., et al., *The bromodomain mediates transcriptional intermediary factor 1alpha -nucleosome interactions.* J Biol Chem, 2002. **277**(52): p. 50318-25). (*See*, paragraph 7)

C. Regarding the scope of proteins binding to a bromodomain

In contrast to these teachings, the Examiner asserts that the present application provides only teachings as to the interaction of an acetylated Tat protein with the bromodomain of P/CAF, and that certain peptides comprising an acetylated lysine are also able to bind the P/CAF bromodomain. The Examiner alleges that these teachings provide no guidance as to what proteins the RING3 bromodomains may interact with, or as to effects of such interaction (if any) on either HIV replication or cancel cell growth. Nor does the application provide such teachings for any of the other bromodomain containing proteins that may fall within the scope of the formula of SEQ ID NO:3.

The Examiner further asserts that the teachings of Mujtaba, *et al.*, (Exhibit B in the Response) indicate on page 583 that many of the residues involved in, and necessary for, P/CAF binding to Tat are not shared among the various other bromodomains of other proteins. Based on such teachings, those in the art would have no grounds for accepting

that the binding of P/CAF to Tat is representative of the ability of bromodomains in general to do so.

Applicants respectfully submit that the patent law does not require any number of species to describe a genus. Nonetheless, Applicants submit herewith the Declaration of Dr. Ming-Ming Zhou pursuant to 37 C.F.R. 1.132 wherein the Declarant clarifies that he is aware of many proteins that have been shown to interact with the bromodomain of another protein. Representative examples include nucleosomal core histones H3, H4, H2A and H2B, each of which has multiple known lysine acetylation sites. In addition, other proteins including cellular proteins of p53 (Mujtaba, S., et al., *Structural mechanism of the bromodomain of the coactivator CBP in p53 transcriptional activation.* Mol Cell, 2004. **13**(2): p. 251-63); NF-κB (Greene, W.C. and L.F. Chen, *Regulation of NF-kappaB action by reversible acetylation.* Novartis Found Symp, 2004. **259**: p. 208-17; discussion 218-25) and HIF1α (Chun, Y.S., et al., *Phorbol ester stimulates the nonhypoxic induction of a novel hypoxia-inducible factor 1alpha isoform: implications for tumor promotion.* Cancer Res, 2003. **63**(24): p. 8700-7) interact with a bromodomain of another protein. (*See*, paragraph 6) In view of this wealth of information in the art, it is clear that one of skill in the art has a wealth of bromodomains and their corresponding ligand at his or her disposal. As such, a skilled artisan may practice the invention without undue experimentation.

D. Regarding binding to lone acetylated lysine and scope of acetyl lysine compounds

The Examiner further alleges that while these claims are drawn to peptides useful for the screening of inhibitors of interaction between a bromodomain and an acetylated lysine, the application teaches that the bromodomain actually tested was not able to bind to a lone acetylated lysine. (*citing*, page 68). Further, the Examiner contends that the application provides rationale for such a lack of binding that would indicate that no bromodomain according to the formula of SEQ ID NO: 3 would be capable of binding such lone acetylated lysines (*citing*, pages 68-69). In view of the teachings in the application that a lone acetyl lysine does not bind to the bromodomains, the Examiner

asserts that the application is not enabling for peptides useful for the screening of inhibitors of such binding.

The Examiner admits that the art and the application teach that the bromodomain of P/CAF binds to an acetylated lysine on Tat, and that this acetylation is required for Tat-P/CAF binding. However, the Examiner contends that it is not clear that any acetyl-lysine would be capable both of binding to P/CAF, or of inhibiting Tat-P/CAF interaction. The Examiner cites to Zeng, *et al. FEBS Letters* 513:124-128 for the proposition that the bromodomains do not interact solely with the acetyl-lysine, but that the specificity of such binding also relies on the presence of other residues flanking the acetyl-lysine. Thus, it is not clear that the presence of any acetyl-lysine analog would be sufficient to overcome the preferential binding of Tat to P/CAF.

Applicants respectfully submit that the Examiner is incorrect factually. Applicants submit herewith the Declaration of Dr. Ming-Ming Zhou pursuant to 37 C.F.R. 1.132 wherein the Declarant clarifies that as reported in the specification of the above-referenced patent application, some bromodomains may not bind to the free amino acid acetyl-lysine alone. This may be due to to the charged amino and/or carboxyl groups of the amino acid lysine that are adjacent to its acetyl moiety. However, bromodomains do in fact interact with and bind to an acetyl-lysine residue when it is presented in a polypeptide sequence such as those in proteins. In latter cases, these charged groups may be naturalized due to polypeptide connectivity. Hence, the acetyl lysine may be necessary for bromodomains to bind to a particular portion of a protein. (*See*, paragraph 8)

E. Regarding inhibiting HIV replication

Furthermore, the Examiner alleges that while the application discloses examples of compounds that are "particularly good candidates" for preventing HIV replication, the application nowhere provides evidence that compounds identified using the claimed peptide would be capable of preventing HIV replication. Other than the suggestion of acetyl-lysine analogs as compounds that may be identified and that may have the ability

to inhibit certain necessary functions of HIV and disclosure of the assay, the application provides no other guidance with respect to what other compounds may perform the requisite functions, or any evidence that any compounds identified through the use of disclosed method (using the claimed peptides) would prevent HIV replication.

According to the Examiner, the teachings in the art indicate that the identification of a desired target, and method for screening for compounds that perform the identified function, is not sufficient to allow those in the art to practice the claimed methods of treating HIV infection. Rather, the art indicates several challenges being faced and indicates an acceptance in the art that HIV therapy is unpredictable. Allegedly, there is insufficient evidence to demonstrate that those in the art would be able to use individual drugs according to the claims to prevent HIV infection.

Applicants herein change the claim language to remove the recitation regarding HIV replication. While some bromodomains may in fact be implicated in such replication, that is not the intended sole purpose of the claims. As such, it is believed that the rejection is moot.

F. Regarding inhibiting tumor cell growth

The claims have been amended to read on peptides useful for screening for inhibitors that may be used to "inhibit tumor cell growth." According to the Examiner, the application provides antecedent basis support for embodiments wherein the inhibitor is useful for the treatment of cancers (page 20), but there is no support in the application for embodiments wherein the inhibitors identified by the disclosed methods may be used to "inhibit tumor cell growth". This may be overcome amending the claims accordingly and providing support for enablement, if available.

Further, the application exemplifies only one of the other disclosed peptides with cancer - the CBP bromodomain. Allegedly, the application provides no guidance as to which other of the peptides falling within SEQ ID NO: 3 would be useful for identifying inhibitors of cancer growth. The application neither identifies specific proteins that are

associated with cancers nor provides any guidance as to other functions of such other proteins.

The Examiner says that the art teaches that different bromodomain containing proteins perform different functions (*citing*, Jeanmougin, *et al.*, *Trends Biochem Sci* 22: 151-153). Further, According to the Examiner, the art also teaches that different bromodomains in the same proteins may also perform different functions. *citing* Guo, *supra,* pages 151-152. Allegedly, the fact that two of the indicated bromodomains have been shown to be associated with certain cancers does not, in view of the different activities of the various bromodomains, establish that any protein comprising a ZA loop within the formula of SEQ ID NO: 3 would also have such an association and be useful for the identification of cancer growth inhibitors. The Examiner alleges that as the application provides insufficient guidance as to which bromodomains are associated with cancers, and as to which would be useful for the identification of inhibitors for those cancers, and in view of limited teachings in the art, and uncertainty in the art as to the effects of inhibiting bromodomain/ligand interactions on cancer, the application fails to enable the full scope of the claimed peptides.

Applicants herein change the claim language to remove the recitation regarding tumor cell growth. While some bromodomains may in fact be implicated in such growth, that is not the intended sole purpose of the claims. As such, it is believed that the rejection is moot.

Regarding Written Description

In addition, the Examiner alleges that the application does not provide written description for the genus of peptides that fall within the formula of SEQ ID NO: 3, useful for identification of inhibitors of HIV replication and tumor cell growth. The Examiner asserts that support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In the present case, the application provides several examples of peptides falling within the scope of SEQ ID NO.: 3. The

application also provides examples of ligands for two of these peptides. Of the disclosed peptides, the applicant has disclosed one as useful for identifying inhibitors of HIV replication (the P/CAF peptide), and one as potentially useful for the inhibition of cancers (the CBP peptide). However, the Examiner contends that the application does not demonstrate that every peptide according to SEQ ID NO: 3 is capable of the indicated uses. While SEQ ID NO.: 3 identifies a common sequence to many of the disclosed peptides, there has been no correlation drawn between the presence of the sequence and the utility of the peptide in the identification of inhibitors of either cancer growth or HIV replication.

Applicant respectfully traverses the Examiner's rejection and asserts that the support for the role of the bromodomain and its interaction with the acetyl lysine of the Tat protein in HIV can be found on page 21, lines 18-30. More importantly, the application provides evidence that acetylated lysine 50 of Tat specifically binds to the bromodomain of P/CAF. The Examiner's attention is drawn to Figures 5-10 and the results of these experiments, which are shown on page 77. This information, taken together with the fact that Tat is tightly regulated by lysine acetylation, and that HIV-1 Tat transcriptional activity is absolutely required for productive HIV viral replication is supportive of a role for this bromodomain as a drug target for blocking HIV replication in cells.

A ligand for a bromodomain is defined on page 48, lines 22-23, wherein it states:

"A compound is identified as a potential ligand if it binds to the ZA loop of the bromodomain."

As shown on page 51, lines 25-28:

"In a particular embodiment of the present invention the bromodomain-ligand complex is the Tat-P/CAF complex and the compound identified by the screen can used to prevent, retard the progression, treat and/or cure AIDS."

Applicant further asserts that Example 1 on pages 52-62 supports the enablement of the ZA loop of the bromodomain binding to its ligand, which in the matter of the present application is an acetylated lysine, such as that found in acetyl-histamine.

Furthermore, agents that can inhibit the binding of the bromodomain with its binding partner/ligand can be found on page 8, lines 29-32, continuing onto page 9, lines 1-8:

"The present invention further provides agents that can inhibit the binding of a bromodomain with a protein comprising an acetyl-lysine. In one embodiment the agent is ISYGR-AcK-KRRQRR (SEQ ID NO:4). In another embodiment the agent is ARKSTGG-AcK-APRKQL (SEQ ID NO:5). In still another embodiment the agent is QSTSRHK-AcK-LMFKTE (SEQ ID NO:6). In yet another embodiment the agent is an analog of acetyl-lysine (see Figures 12 and 13). One particular analog of acetyl-lysine is acetyl-histamine. In still another embodiment the agent is an antibody that recognizes an acetyl-lysine of a protein binding partner of a bromodomain. In a preferred embodiment the agent is an antibody raised against a ZA loop of a bromodomain. These agents can be used as pharmaceuticals in compositions that contain a pharmaceutically acceptable carrier for example, or in the various drug assays of the present invention, serving as controls to demonstrate specificity."

Furthermore, Applicants have provided previously a declaration under 37 CFR 1.132 which includes additional support for compounds identified by the methods described herein. The Examiner's attention is drawn to the inventor's declaration whereby compounds have been identified on the basis of the bromodomain and ZA loop sequences and coordinates provided in the instant application.

In addition, Applicants herein remove the offending recitations that expressly set forth the utility of the invention as useful for screening inhibitors that are in turn useful for preventing HIV replication or tumor cell growth. Applicants clearly describe bromodomains that are useful for screening for the compounds that inhibit the binding of the bromodomain to acetylated lysine residue of a peptide. Based on the foregoing, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. 102

1. Yang et al.

The Examiner maintains the rejection of claims 5 and 6 under 35 U.S.C. 102(b) as being anticipated by Yang, *et al.* More particularly, the claims have been amended to read on a peptide comprising a ZA loop of a bromodomain, wherein the ZA loop consists of SEQ ID NO: 3. According to the Examiner, the claim places no limitations on what other sequences may be present in the peptide other than the ZA loop. Thus, the claim reads on any peptide comprising a sequence according to SEQ ID NO: 3. According to the Examiner, Yang teaches a fusion protein of P/CAF with a FLAG epitope, wherein the polypeptide includes SEQ ID NO.:3. Allegedly, the peptide of Yang meets the structural limitations of the claimed peptides, e.g., the peptides of SEQ ID NO: 3.

The Examiner alleges that while claim 5 has been amended to insert a "consisting" phrase, this is not a complete description of what is claimed. The claim is directed to any peptide comprising a ZA loop consisting of SEQ ID NO: 3. The claim does not however provide any limitation as to what the other sequences of the peptide may comprise. Thus, the claims read on any peptide comprising SEQ ID NO: 3. Yang allegedly teaches such a peptide because the claim is not limited to peptides consisting of SEQ ID NO: 3.

Applicants respectfully traverse the Examiner's rejection and assert that Yang et al. do not teach or suggest that the ZA loop of the P/CAF bromodomain, in particular, the synthetic ZA loop of SEQ ID NO: 3, and the bromodomain sequence of SEQ ID NO: 19. More particularly, Yang et al do not teach or suggest the use of this synthetic ZA loop sequence as provided by the present inventors for use in identifying drugs that inhibit the interaction between the bromodomain of P/CAF and the Tat. It was only through the teachings of the present application that the particular residues of the ZA loop of the bromodomain were identified as being crucial for the interaction between the bromodomain and the acetylated lysine of the Tat peptide. Furthermore, claims 5 and 7

have been amended to recite "consisting of", rather than "comprising", in both instances of its occurrence such that the sequences claimed no longer read on the sequences taught by Yang et al.

2. Davis and Green

The Examiner also maintains the rejection of claims 5-8 as allegedly anticipated by Davis & Green. The Examiner asserts that the claims read on any peptide comprising a sequence according to the formula of SEQ ID NO: 3. SEQ ID NO: 19 comprises such a sequence. Because Davis and Green teach a peptide comprising this sequence, the reference meets the structural limitations of the claimed peptides.

Applicants respectfully traverse the Examiner's rejection and assert that claims 5 and 6 of the present invention do not read on SEQ ID NO: 19. Furthermore, Denis and Green do not teach or suggest a ZA loop of a bromodomain that may be used for screening inhibitors of the interaction between a bromodomain, such as that in P/CAF and an acetylated lysine of Tat. Applicants assert that the Denis and Green reference does not teach or suggest the use of the crucial amino acid residues necessary for the interaction between P/CAF and acetylated lysine of Tat for identifying inhibitors of this interaction. It was only through the work of the present inventors that such criticality of specific residues for interaction between the ZA loop of the bromodomain and the acetylated lysine of Tat became apparent. Furthermore, claims 5 and 7 have been amended to recite "consisting of", rather than "comprising", in both instances of its occurrence such that the sequences claimed no longer read on the sequences taught by Davis and Green. Based on the foregoing, withdrawal of the rejection is respectfully requested.

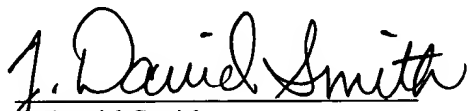
Fees

No fees are believed to be necessary in connection with this response. However, if this is in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

Conclusion

Applicants believe that the foregoing amendments to the claims place the application in condition for allowance. Withdrawal of the rejections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 118, to effect a resolution.

Respectfully submitted,



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